

AMENDMENT AND RESPONSE

Serial Number: 08/913,257

Filing Date: December 5, 1997

Title: ESTERS OF 5-AMINOLEVULINIC ACID AS PHOTSENSITIZING AGENTS IN PHOTOCHEMOTHERAPY

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Dkt: 697.002US1



(I)

wherein,  $R^1$  is alkyl; and each  $R^2$  is independently hydrogen or alkyl;

wherein each alkyl of  $R^1$  and  $R^2$  is optionally substituted by hydroxy, alkoxy, acyloxy, alkoxycarbonyloxy, amino, aryl, oxo or fluoro groups and is optionally interrupted by oxygen atoms; or a salt thereof; and ii) exposing said sites or surfaces to light.

2

~~2~~.(NEW) The method of claim ~~2~~ wherein aryl is phenyl or a monocyclic 5-7 membered heteroaromatic.

3

~~3~~.(NEW) The method of claim ~~2~~ wherein  $R^1$  represents an unsubstituted alkyl group and each  $R^2$  is hydrogen.

4

~~4~~.(NEW) The method of claim ~~2~~ wherein  $R^1$  represents an unsubstituted alkyl group or each  $R^2$  is hydrogen.

5

~~5~~.(NEW) The method of claim ~~2~~ wherein alkyl contains up to 10 carbon atoms.

6

~~6~~.(NEW) The method of claim ~~2~~ wherein the compound is ALA-methyl ester, ALA-ethyl ester, ALA-propyl ester, ALA-hexyl ester, ALA-heptyl ester, or ALA-octyl ester; or a salt thereof.

7

~~7~~.(NEW) The method of claim ~~2~~ wherein the light is in the wavelength region 500-700 nm.

8

~~8~~.(NEW) A pharmaceutical composition comprising a compound of formula I



(I)

wherein, R<sup>1</sup> is alkyl; and each R<sup>2</sup> is independently hydrogen or alkyl;  
wherein each alkyl of R<sup>1</sup> and R<sup>2</sup> is optionally substituted by hydroxy, alkoxy, acyloxy, alkoxycarbonyloxy, amino, aryl, oxo or fluoro groups and is optionally interrupted by oxygen atoms; or a pharmaceutically acceptable salt thereof; together with at least one pharmaceutical carrier or excipient.

<sup>9</sup>  
~~29~~.(NEW) The composition of claim <sup>4</sup>~~28~~ wherein the compound is ALA-methyl ester, ALA-ethyl ester, ALA-propyl ester, ALA-hexyl ester, ALA-heptyl ester, or ALA-octyl ester; or a pharmaceutically acceptable salt thereof.

<sup>10</sup>  
~~30~~.(NEW) The composition of claim <sup>8</sup>~~28~~ further comprising at least one surface-penetration assisting agent, and optionally one or more chelating agents.

<sup>11</sup>  
~~31~~.(NEW) The composition of claim <sup>10</sup>~~30~~ wherein the surface-penetration assisting agent is dimethyl sulfoxide.

<sup>12</sup>  
~~32~~.(NEW) The composition of claim <sup>10</sup>~~30~~ wherein the compound is ALA-methyl ester, ALA-ethyl ester, ALA-propyl ester, ALA-hexyl ester, ALA-heptyl ester, or ALA-octyl ester; or a pharmaceutically acceptable salt thereof.

<sup>13</sup>  
~~33~~.(NEW) A method for in vitro diagnosis of abnormalities or disorders by assaying a sample of body fluid or tissue of a patient, said method comprising:

- i) admixing said body fluid or tissue with a compound of formula I



(I)

wherein, R<sup>1</sup> is alkyl; and each R<sup>2</sup> is independently hydrogen or alkyl;

wherein each alkyl of R<sup>1</sup> and R<sup>2</sup> is optionally substituted by hydroxy, alkoxy, acyloxy, alkoxycarbonyloxy, amino, aryl, oxo or fluoro groups and is optionally interrupted by oxygen atoms; or a pharmaceutically acceptable salt thereof;

- ii) exposing said mixture to light;
- iii) ascertaining the level of fluorescence; and
- iv) comparing the level of fluorescence to control levels.

<sup>14</sup>  
34.(NEW) The method of claim <sup>13</sup>~~33~~ wherein the compound is ALA-methyl ester, ALA-ethyl ester, ALA-propyl ester, ALA-hexyl ester, ALA-heptyl ester, or ALA-octyl ester; or a pharmaceutically acceptable salt thereof.

*B1*  
*Amended*  
35.(NEW) A kit for use in diagnosis or photochemotherapy of disorders or abnormalities of external or internal surfaces of the body comprising:

- i) a first container containing a compound of formula I



(I)

wherein, R<sup>1</sup> is alkyl; and each R<sup>2</sup> is independently hydrogen or alkyl;  
wherein each alkyl of R<sup>1</sup> and R<sup>2</sup> is optionally substituted by hydroxy, alkoxy, acyloxy, alkoxycarbonyloxy, amino, aryl, oxo or fluoro groups and is optionally interrupted by oxygen atoms; or a pharmaceutically acceptable salt thereof;

- ii) a second container containing at least one surface penetration assisting agent; and optionally
- iii) one or more chelating agents contained either within said first container or in a third container.

<sup>119</sup>  
36.(NEW) The kit of claim <sup>15</sup>~~35~~ wherein the compound is ALA-methyl ester, ALA-ethyl ester, ALA-propyl ester, ALA-hexyl ester, ALA-heptyl ester, or ALA-octyl ester; or a pharmaceutically acceptable salt thereof.